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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,084	06/08/2006	Claus Harder	117163.00137	8537

21324 7590 10/05/2009

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EXAMINER	
FRAZIER, BARBARA S	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
10/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/535,084	HARDER ET AL.	
	Examiner	Art Unit	
	BARBARA FRAZIER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-23* is/are pending in the application.

4a) Of the above claim(s) *1-3,8,10,11 and 16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,7,9 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/16/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-4 and 7-23 are pending in this application. Claims 5, 6, 24, and 25 stand canceled. Claims 4 and 7-18 have been amended.

2. Claims 1-3 and 19-23 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/22/08.

3. Claims 8, 10, 11, and 16-18 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/22/08.

4. Claims 4, 7, 9, and 12-15 are examined.

Double Patenting

5. The provisional rejections of claims 4, 7, 9, and 12-15 on the ground of obviousness-type double patenting as being unpatentable over claims 1-6 and 21-24 of copending Application No. 10/706,717; claims 1-3, 5, 7-9, and 16-19 of copending Application No. 10/596,797; claims 1-9 and 11 of copending Application No. 10/908,729; claims 1-4 of copending Application No. 11/221,322 and claims 1-4 of

copending Application No. 11/221,344, have been withdrawn in view of Applicant's Terminal Disclaimers filed 6/19/09.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 4, 7, 9, 12, 13, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "the formulation" in lines 3-4. Claims 9, 12, 13, and 15 similarly recite "the formulation". There is insufficient antecedent basis for this limitation in the claim, as claim 4 has been amended from "a pharmaceutical formulation" to now read "an endoprosthesis" in line 1. Claim 7 depends from claim 4 and does not remedy this deficiency, and therefore is also rejected.

Claim Rejections - 35 USC § 102

8. The rejection of claims 4, 7, and 15 under 35 U.S.C. 102(b) as being anticipated by Stroganov et al (US Patent 3,687,135) is withdrawn in view of Applicant's amendments to claims 4, 7, and 15.

Claim Rejections - 35 USC § 103

9. The rejection of claims 9 and 12-14 under 35 U.S.C. 103(a) as being unpatentable over Stroganov et al (US Patent 3,687,135) is withdrawn in view of Applicant's amendments to claims 9 and 12-14.

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heublein et al (US 2002/0004060).

The claimed invention is drawn to an endoprosthesis comprising one or more of the elements from the group yttrium (Y), neodymium (Nd), or zirconium (Zr), wherein the endoprosthesis is adapted to be implanted in a vascular vessel and adapted to inhibit the proliferation of human smooth muscle cells of the vascular vessel wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel and the formulation includes an at least very substantially biodegradable carrier (see claim 4). Claim 7 is drawn to the a formulation as set forth in claim 4, wherein the carrier is an alloy, selected from the group consisting of magnesium, iron and tungsten alloys.

Heublein et al disclose a medical implant made of a metallic material (abstract), wherein the medical implant may be adapted for a vascular vessel, such as a stent (paragraphs 6 and 10). Vessel supports are able to overcome problems of a permanent implant, including in-stent stenosis (paragraphs 31 and 7), and therefore are adapted to

inhibit the proliferation of human smooth muscle cells of the vascular vessel. The implants are made of biodegradable material having at the same time advantageous mechanical properties (paragraph 11); said biodegradability reasonably reads on being adapted for "intravascular liberation" after implantation in a vascular vessel. Heublein et al further disclose that magnesium is preferred as the main constituent (paragraphs 13, 15, and 37) with a subsidiary constituent such as zirconium (paragraph 14), and advantageous decomposition times have furthermore been afforded by materials with magnesium as main constituent and 1-4% rare earths, in particular neodymium (paragraphs 15 and 17).

Heublein et al do not specifically exemplify the combination of zirconium or neodymium with a magnesium carrier.

However, it would have been obvious to a person having ordinary skill in the art at the time the invention was made to select zirconium or neodymium with the magnesium carrier; thus arriving at the claimed invention. One skilled in the art would have been motivated to do so, with a reasonable expectation of success, because Heublein et al fairly teach and suggest the use of zirconium or neodymium as the subsidiary constituent, and magnesium as the main constituent. Thus, it would be within the purview of the skilled artisan to select either zirconium or neodymium with the magnesium carrier by routine experimentation, in order to optimize properties of the resultant formulation, such as stability and controlled degradation.

Response to Arguments

12. Applicant's arguments filed 6/19/09 have been fully considered but they are not persuasive.

Applicants argue that one of ordinary skill in the art would not equate a lack of stimulation of smooth muscle cell growth (achieved by the temporary presence of a degradable stent) with actual inhibition of smooth muscle cell proliferation. The Examiner disagrees; a lack of stimulation of smooth muscle cell growth is equivalent to inhibition of smooth muscle cell proliferation (growth). Furthermore, one skilled in the art would reasonably expect the formulation taught by Hueblein et al to inhibit smooth muscle cell growth, since the components and amounts taught in the formulation of Heublein et al are the same as those of the claimed invention, and Applicants have provided no objective evidence that it would not. "The arguments of counsel cannot take the place of evidence in the record." *In re Schulze*, 346 F.2d 600, 145 USPW 716,718 (CCPA 1965), *In re Huang*, 40 USPQ 2d 1685 (Fed. Cir. 1996), *In re De Blauwe et al*., 222 USPQ 191, (Fed. Cir. 1984).

Applicants argue that the compositions disclosed in Heublein include a wide variety of potential components but Heublein provides no actual guidance as to advantages or disadvantages of any of them, including inhibition of smooth muscle cell growth. Applicants argue that “other metal and rare earths” are also disclosed as potential components, and a magnesium alloy containing up to 40% lithium is preferred.

This argument is not persuasive because disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or

nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Since Hueblein et al fairly teach and suggest the incorporation of neodymium and/or zirconium in its magnesium-based alloy, it would be within the purview of the skilled artisan to select either zirconium or neodymium with the magnesium carrier by routine experimentation, in order to optimize properties of the resultant formulation, such as stability and controlled degradation.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

13. Claims 9 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heublein et al as applied to claims 4 and 7 above, and further in view of *The Columbia Electronic Encyclopedia*, 6th ed., 2007.

Claim 9 of the claimed invention is drawn to a formulation as set forth in claim 4, wherein the formulation contains Y in a quantitative proportion of between 3.7 and 5.5% by weight with respect to the total weight of the formulation (claim 9).

The invention of Heublein et al is delineated above (see paragraph 22). Heublein et al further teach that the formulation may contain 0- 5% rare earths (paragraphs 16 and 21).

Heublein et al do not teach that the rare earths may be yttrium.

However, one skilled in the art would reasonably envisage the use of yttrium from the disclosure of "rare earths" in Heublein et al. As evidence, *The Columbia Electronic Encyclopedia*, 6th ed., defines "rare earths" as a group of metals including yttrium (see citation at http://www.infoplease.com/ce6/sci/A0841162.html). Therefore, it would be within the purview of the skilled artisan to select yttrium as the rare earth in the formulation of Heublein et al by routine experimentation, in order to optimize the properties of the resultant formulation, including efficacy, stability, and rate of degradation. Regarding the amount of yttrium, the amount range taught by Heublein et al overlaps that of the claimed invention; one skilled in the art would be motivated to manipulate the amount of yttrium from within said ranges by routine experimentation, in order to optimize the properties of the resultant formulation, including efficacy, stability, and rate of degradation.

Regarding claim 15, one skilled in the art would reasonably expect the formulation taught by Heublein et al to provide an yttrium concentration in the region of the human smooth muscle cells to be treated of between 200uM and 2 mM, as recited in the claimed invention, since the components and amounts taught in the formulation of Heublein et al are the same as those of the claimed invention.

Response to Arguments

14. Applicant's arguments filed 7/16/09 have been fully considered but they are not persuasive.

Applicants argue that neither reference provides a teaching or suggestion of delivery of yttrium to the smooth muscle cells in the range of 200 uM and 2 mM as recited in claim 15. Applicants argue that rare earth elements are only generally disclosed by Heublein as one of many potential components, and the Examiner must rely on The Columbia Electronic Encyclopedia for the teaching that yttrium is a rare earth element. Applicants also argue that the actual concentration of yttrium delivered will depend on the rate of degradation of the overall alloy containing the yttrium, and neither of the cited references provides one of ordinary skill in the art with any guidance on the desirability of delivery of yttrium at all, much less at the specified concentrations.

This argument is not persuasive. Heublein et al teach that the amount of rare earths may be less than 5% (paragraph 16). This amount overlaps that of the claimed invention, and one skilled in the art would be motivated to manipulate the amount of yttrium from within said ranges by routine experimentation, in order to optimize the properties of the resultant formulation, including efficacy, stability, and rate of degradation (for example, see paragraph 14 of Heublein). The Examiner further notes that the rejection is not based on the teachings of Heublein alone, but rather Heublein in view of The Columbia Electronic Encyclopedia, which teaches that yttrium is a known rare earth metal. Since the formulation of the combined references teaches the same components and amounts as that of the claimed invention, one skilled in the art would

reasonably expect the formulation of the combined references to have the same yttrium concentration in the region of the human smooth muscle cells as that of the claimed invention.

15. Claims 9 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heublein et al as applied to claims 4 and 7 above, and further in view of Tikhova et al (GB 1378281, cited by Applicants in IDS filed 7/16/09) and ASM International Metals Handbook (Vol. 2, 1997, cited by Applicants in IDS filed 7/16/09, hereinafter "ASM Handbook").

The invention of claims 9 and 15 is delineated above (see paragraph 13). Claims 12-14 are further drawn to an endoprosthesis as set forth in claim 7, wherein the formulation is a magnesium alloy containing Y, rare earth without Y such as Nd, and remaining elements such as Zr, such as a WE43 alloy.

The invention of Heublein et al is delineated above (see paragraph 11). While Heublein et al generally teach the presence of rare earths in its magnesium-based alloy, Heublein et al do not specifically teach the presence of yttrium with neodymium and zirconium.

Tikhova et al teach that magnesium-based alloys containing yttrium, neodymium and zirconium, in amounts comparable to that of the claimed invention, are known (col. 2, lines 43-48). Tikhova et al further teach that, due to the presence of yttrium and neodymium, the alloy exhibits favorable combination of high creep resistance and strength, leading to improved thermal stability (col. 2, lines 49-54), and zirconium is

efficient for the formation of a fine-grained structure, which contributes not only to enhancement of mechanical properties in respect of short-term stress but to substantial improvement in technological casting properties of the alloy (col. 2, lines 55-60).

ASM Handbook teaches that the alloy WE43 is a known Mg-Y-Nd-Zr alloy (disclosure).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to use a Mg-Y-Nd-Zr alloy such as WE43 in the implant of Heublein et al; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because the use of said magnesium-based alloy provides the advantageous properties of high creep resistance and strength, improved thermal stability, enhancement of mechanical properties in respect of short-term stress and improved technological casting properties of the alloy, as taught by Tikhova et al. One would reasonably expect success from the use of a Mg-Y-Nd-Zr alloy such as a WE43 alloy in the implant of Heublein et al because Heublein et al fairly teach and suggest that its magnesium-based alloys may contain rare earths, as well as zirconium and neodymium.

Regarding claim 15, one skilled in the art would reasonably expect the formulation taught by the combined references to provide an yttrium concentration in the region of the human smooth muscle cells to be treated of between 200uM and 2 mM, as recited in the claimed invention, since the components and amounts taught in the formulation of the combined references are the same as those of the claimed invention.

Conclusion

16. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 7/16/09 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Sharmila Gollamudi Landau/
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